

PANDUAN PRAKTIKUM BLOK XIV KARDIOVASKULAR

EDISI PERTAMA

2020



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PRAKTIKUM I

ANTI HIPERTENSI

I. Tujuan

Setelah pelaksanaan praktikum mahasiswa harus dapat menjelaskan pengobatan Antihipertensi berdasarkan sasaran pengobatan.

II. Capaian Pembelajaran

Setelah pelaksanaan praktikum mahasiswa harus dapat menjelaskan :

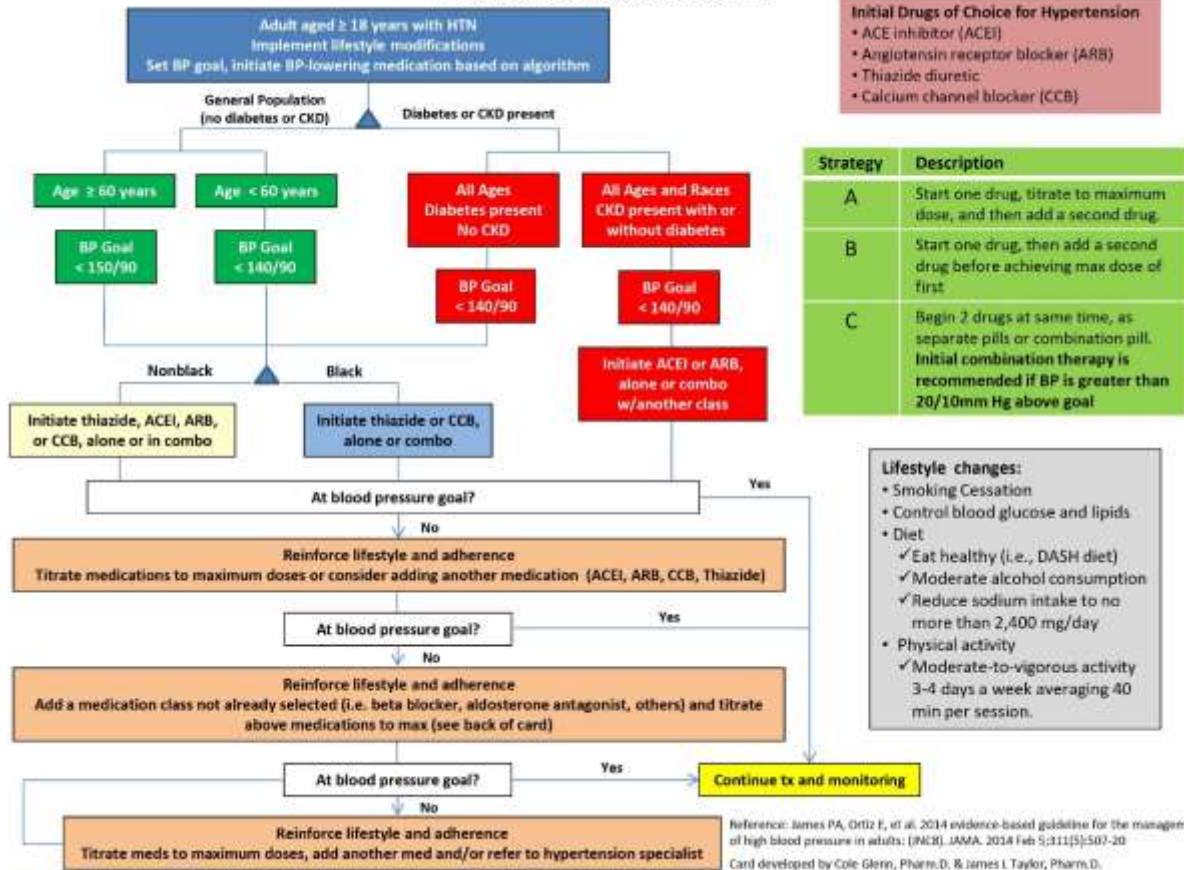
1. Golongan Obat Antihipertensi dan contohnya
2. Tiga Panduan/ Pedoman dalam terapi hipertensi
3. Panduan Algoritma JNC 8 dalam terapi hipertensi
4. Golongan Obat Antihipertensi sebagai tujuan pemberian monoterapi dan obat pilihan monoterapi
5. Golongan Obat Antihipertensi sebagai tujuan pemberian kombinasi terapi antihipertensi dan obat pilihan kombinasi terapi yang tepat

III. Topik

Telaah Jurnal dan Melihat Youtube :

1. [Pharmacology - HYPERTENSION & ANTIHYPERTENSIVES \(MADE EASY\) - YouTube](#)
2. Panduan Algoritma JNC 8 dalam terapi hipertensi
3. Jurnal 1 : Evaluation of Antihypertension Drug Prescription Pattern, Rationality, and Adherence to Joint National Committee-8 Hypertension Treatment Guidelines among Patient Attending Medicine OPD in a Tertiary Care Hospital
4. Jurnal 2 : Gambaran Pola Penggunaan Obat Antihipertensi pada Pasien Hipertensi di Instalasi Rawat Inap RSUP Sanglah Denpasar tahun 2016.

JNC 8 Hypertension Guideline Algorithm



Compelling Indications	
Indication	Treatment Choice
Heart Failure	ACEI/ARB + BB + diuretic + spironolactone
Post-MI/Clinical CAD	ACEI/ARB AND BB
CAD	ACEI, BB, diuretic, CCB
Diabetes	ACEI/ARB, CCB, diuretic
CKD	ACEI/ARB
Recurrent stroke prevention	ACEI, diuretic
Pregnancy	labetalol (first line), nifedipine, methyldopa

Hypertension Treatment

Beta-1 Selective Beta-blockers – possibly safer in patients with COPD, asthma, diabetes, and peripheral vascular disease:

- metoprolol
- bisoprolol
- betaxolol
- acebutolol

Drug Class	Agents of Choice	Comments
Diuretics	HCTZ 12.5-50mg, chlorthalidone 12.5-25mg, indapamide 1.25-2.5mg, triamterene 100mg K ⁺ sparing – spironolactone 25-50mg, amiloride 5-10mg, triamterene 100mg furosemide 20-80mg twice daily, torsemide 10-40mg	Monitor for hypokalemia Most SE are metabolic in nature Most effective when combined w/ ACEI Stronger clinical evidence w/chlorthalidone Spironolactone – gynecomastia and hyperkalemia Loop diuretics may be needed when GFR <40mL/min
ACEI/ARB	ACEI: lisinopril, benazepril, fosinopril and quinapril 10-40mg, ramipril 5-10mg, trandolapril 2-8mg ARB: candesartan 8-32mg, valsartan 80-320mg, losartan 50-100mg, olmesartan 20-40mg, telmisartan 20-80mg	SE: Cough (ACEI only), angioedema (more with ACEI), hyperkalemia Losartan lowers uric acid levels; candesartan may prevent migraine headaches
Beta-Blockers	metoprolol succinate 50-100mg and tartrate 50-100mg twice daily, nebivolol 5-10mg, propranolol 40-120mg twice daily, carvedilol 6.25-25mg twice daily, bisoprolol 5-10mg, labetalol 100-300mg twice daily,	Not first line agents – reserve for post-MI/CHF Cause fatigue and decreased heart rate Adversely affect glucose, mask hypoglycemic awareness
Calcium channel blockers	Dihydropyridines: amlodipine 5-10mg, nifedipine ER 30-90mg, Non-dihydropyridines: diltiazem ER 180-360 mg, verapamil 80-120mg 3 times daily or ER 240-480mg	Cause edema; dihydropyridines may be safely combined w/ B-blocker Non-dihydropyridines reduce heart rate and proteinuria
Vasodilators	hydralazine 25-100mg twice daily, minoxidil 5-10mg terazosin 1-5mg, doxazosin 1-4mg given at bedtime	Hydralazine and minoxidil may cause reflex tachycardia and fluid retention – usually require diuretic + B-blocker Alpha-blockers may cause orthostatic hypotension
Centrally-acting Agents	clonidine 0.1-0.2mg twice daily, methyldopa 250-500mg twice daily guanfacine 1-3mg	Clonidine available in weekly patch formulation for resistant hypertension

Evaluation of Antihypertensive Drug Prescription Patterns, Rationality, and Adherence to Joint National Committee-8 Hypertension Treatment Guidelines among Patients Attending Medicine OPD in a Tertiary Care Hospital

Chandra Narayan Gupta¹, Akul SK², Sugata Mahapatra³, Apala Lahiri⁴, Kausik Maji⁵, Sukanta Sen⁶

ABSTRACT

Introduction: The increasing prevalence of hypertension is attributed to population growth, ageing and behavioural risk factors, such as unhealthy diet, harmful use of alcohol, lack of physical activity, excess weight and exposure to persistent stress. The present study was conducted to study on various facets of antihypertensive drugs prescribing at present scenario at Dr B.C. Roy Hospital, Haldia, and with objectives of studying prescribing patterns and rationality of antihypertensive drugs in essential hypertension with or without specific co-morbid conditions and to check compliance of treatment as per JNC-8 hypertension treatment guidelines in the outpatients attending the Department of Medicine.

Material and Methods: Data regarding anti-HTN monotherapy and combination therapy was recorded. Evaluation for rational drug therapy by evaluating average number of drugs per prescription, fixed dose combination (FDC) prescription rate, prescription laying down importance of lifestyle management, prescription with defined anti-HTN goals, prescriptions with correct dose strength and dosage schedule was evaluated.

Results: Out of 100 hypertensive patients under evaluation 67 was males (67%) with a M:F ratio of 2.03:1. Mean SBP was slightly higher in male patients. Hypertension was classified according to JNC-8 guidelines and found 22 (22%) (Pre-hypertension/pre-HTN), 57 (57%) (Stage 1 hypertension), and 13% (stage 2 hypertension) cases. Dyslipidemia was noted much more common associated disorders among newly diagnosed hypertensive of either sex.

Conclusion: Diuretics (8%) were most widely prescribed drugs followed by ARBs (6%), ACE Inhibitors (5%) and calcium channel blockers (4%) as monotherapy. Adherence of JNC 8 guidelines among all study hypertensive participants while prescribing medications varied between 62% to 92%, with an average of 75%. None of the prescriptions mentioned ban drug formulation(s). Still 15% of the prescriptions had suggested combined drugs with debated rationality formulations.

Keywords: Antihypertensive Drug Prescription Patterns, Rationality, Joint National Committee-8, Hypertension Treatment Guidelines, Patients Attending Medicine OPD

INTRODUCTION

Hypertension is defined as a systolic blood pressure (SBP) of 140 mm Hg or more, or a diastolic blood pressure (DBP) of 90 mm Hg or more, or taking antihypertensive medication.¹ Globally, an estimated 26% of the world's

population (972 million people) has hypertension, and the prevalence is expected to increase to 29% by 2025.² HTN exerts a substantial public health burden on cardiovascular health status and healthcare systems in India. Blood pressure control is essential to prevent end-organ complications, such as stroke, myocardial infarction, heart failure, or kidney disease.³

Hypertension (HTN) is the most common condition seen in primary health care setting and leads to myocardial infarction, stroke, renal failure, and death if not detected early and treated appropriately. There are significant health and economic gains attached to early detection, adequate treatment and good control of hypertension. High blood pressure (BP) is ranked as the third most important risk factor for attributable burden of disease in south Asia (2010).⁴ In 2008, worldwide, approximately 40% of adults aged 25 and above had been diagnosed with hypertension; the number of people with the condition rose from 600 million in 1980 to 1 billion in 2008.⁵ Study had shown that HTN is directly

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How to cite this article: Chandra Narayan Gupta, Akul SK, Sugata Mahapatra, Apala Lahiri, Kausik Maji, Sukanta Sen. Evaluation of antihypertensive drug prescription patterns, rationality, and adherence to joint national committee-8 hypertension treatment guidelines among patients attending medicine OPD in a tertiary care hospital. International Journal of Contemporary Medical Research 2019;6(10):J31-J37.

DOI: <http://dx.doi.org/10.21276/ijcmr.2019.6.10.42>

responsible for 57% of all stroke deaths and 24% of all coronary heart disease (CHD) deaths in India.⁶

According to JNC 8 recommendations the general population, initial antihypertensive treatment should include a thiazide diuretic, calcium channel blocker, ACE inhibitor, or ARB in the general non-black population or a thiazide diuretic or calcium channel blocker in the general black population.⁷ The three guidelines that have been instrumental in recent time to have implications in clinical practice in management of hypertension include:

1. ESH guidelines
2. ASH / ISH guidelines
3. JNC VIII Panel Recommendation

Although these guidelines and recommendations have been quite comprehensive there still remain some unanswered questions. The Eighth Joint National Committee (JNC 8) recently released evidence-based recommendations on treatment thresholds, goals, and medications in the management of hypertension in adults.⁷

The Joint National Committee (JNC-8) is considered the "gold standard" consensus guidelines for the management of hypertension. About goals of older individuals, a 2014 report from panel members of the Eighth Joint National Committee (JNC8) suggested that in patients aged ≥ 60 years, blood pressure should be targeted to $<150/90$ mm Hg.⁷ SPRINT trial results may eventually contribute to a revision of JNC8 recommendations, but for now most experts urge a go-slow treatment approach and continued adherence to the 2014 guidelines.⁸

To treat hypertension with or without co-morbid conditions various guidelines have been issued. Report of Eight Joint National Committee (JNC 8)⁷ and guidelines by WHO-International Society of Hypertension (WHO-ISH)⁹ are important ones. These guidelines are important tools to improve the clinical approach of the physician in the daily treatment. They are aimed to provide indications for clinical practice based on rigorous scientific evidence. However, their use in decision making in clinical practice is largely neglected by physicians.^{10,11} Patients want to be assured that HTN treatment will reduce their disease burden, while clinicians want guidance on hypertension management using the best scientific evidences. Keeping in view, the present study will be conducted to study on various facets of antihypertensive drugs prescribing at present scenario at Dr B.C. Roy Hospital, Haldia, a tertiary care teaching hospital and with objectives of studying prescribing patterns and rationality of antihypertensive drugs in essential hypertension with or without specific co-morbid conditions and to check compliance of treatment as per JNC-8 hypertension treatment guidelines in the outpatients attending the Department of Medicine.

MATERIAL AND METHODS

A cross-sectional, observational study was carried out in the Outpatient Department of Medicine, in Dr B C Roy Hospital associated with ICARE Institute of Medical Sciences & Research, Haldia, West Bengal for 3 months.

Permission from the Institutional Ethics Committee was obtained before starting research work. Subjects and their accompanying family members was interviewed by pre-structured questionnaire, and past and present prescriptions and case notes, where available, was reviewed. All decisions relating to management of the patient including drugs and investigations was taken by the treating physician only. Investigator did not interfere in the management of patient and only observed the proceedings.

Antihypertensive drugs were categorized according to the eighth report of the JNC on prevention, detection, evaluation, and treatment of high blood pressure (JNC-8).⁷ Data regarding anti-HTN mono-therapy and combination therapy was recorded. Evaluation for rational drug therapy by evaluating average number of drugs per prescription, fixed dose combination (FDC) prescription rate, prescription laying down importance of lifestyle management, prescription with defined anti-HTN goals, prescriptions with correct dose strength and dosage schedule was evaluated. Number of prescriptions mentioning duration of therapy, over prescribing, banned drug formulation, debated rationality or irrational combinations, generic, and brand names used was also captured. The prescriptions was collected by an me by clicking the picture by mobile outside the medical outpatient department and interviewing the HTN patients without the knowledge of prescriber to avoid any bias after taking verbal consent and after due administrative and Institutional Ethics Committee permission.

Inclusion criteria

1. Subjects who was suffering from essential hypertension and prescribed antihypertensive at Medicine O.P.D.
2. Patients from all age groups and both the sexes will be included
3. Hypertensive patients with co-morbidities like diabetes mellitus, ischemic heart diseases, congestive heart failure and chronic renal diseases will also be included in the study
4. Those who understood the purpose of the study and are ready to provide information regarding their health status and those who signed an informed consent document.

Exclusion criteria

1. Subjects not agreeing to participate
2. Suffering from any serious disease such as hypertensive emergencies, unstable coronary heart disease, acute myocardial infarction, acute left ventricular failure, advanced kidney or liver failure, and cerebral stroke
3. Any condition resulting in severe learning disability (e.g. brain injury) or
4. Those unable to comprehend for other reasons will be excluded from the study.

A total of 100 hypertensive patients was studied because time and facility constraints. The study was commenced after obtaining approval from institutional ethics committee and was continued for a span of 3 months in the Medicine Out-Patient Department (OPD) of Dr. B C Roy Hospital, Haldia, West Bengal. Data was analyzed at the end of study.

All statistical calculations were performed using Statistical Package for Social Science (SPSS), version 20.0. Data were expressed in n (%). A *P*-value of <0.05 was considered as statistically significant.

RESULTS

One hundred prescriptions were collected randomly in the duration of 3 months to assess medication adherence as per JNC 8 guidelines among Indian hypertensive patients attending Medicine OPD of a tertiary care teaching hospital, Haldia, West Bengal. The demographic and clinical characteristics were shown in Table 1. Out of 100 hypertensive patients under evaluation 67 was males (67%) with a M:F ratio of 2.03:1. Mean age among male participants was less (55.29±16.48) in comparison to female hypertensive (59.30±11.55). Mean SBP was slightly higher in male patients. Majority of the hypertensive patients in either sex was in the 40-60 yrs age group followed by age group above 60 years. The highest number of male hypertensive patients 40 (59.7%) [n=67] belonged to the age group of 40-60 years while the highest number of female hypertensive patients 17 (51.51%) [n=33] belonged to the age group of 40-60 years suggesting the earlier onset of hypertension in males than in females in this particular area where the study has been conducted (Table 1).

In male patients stage 1 HTN was observed in 55.22% followed pre-HTN (22.38%) and stage 2 HTN (13.43%).

In female participants it was observed that stage 1 HTN (60.60%) followed by pre-HTN (21.21%) and stage 2 HTN (12.12%) (Table 1). Hypertension was classified according to JNC-8 guidelines and found 22 (22%) (Pre-hypertension/pre-HTN), 57 (57%) (Stage 1 hypertension), and 13% (stage 2 hypertension) cases. The mean systolic blood pressure was 151.8±18.68 mm Hg (males) and 150.4±16.03 mm Hg (females) (Table 1).

Diabetes mellitus (11.94%, males; 12.12%, females), other cardiovascular diseases (8.95%, males; 18.18%, females), acid peptic disease (23.88%, males; 27.27%, females), obesity (11.94%, males; 18.18%, females), and dyslipidemia (40.29%, males; 42.42%, females) are the most common co-morbidities in hypertension patients (Table 2/Fig. 1). Dyslipidemia was noted much more common associated disorders among newly diagnosed hypertensive of either sex.

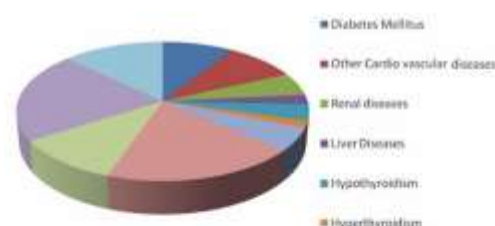


Figure-1: Co-morbid conditions among hypertensive subjects

Characteristics	Males [n=67]	Females [n=33]	P value
Age (Mean ± SD)	55.29±16.48	59.30±11.55	=0.2132
<40 years	08 (11.94%)	03 (9.09%)	= 0.6700
40-60 years	40 (59.7%)	17 (51.51%)	= 0.4390
Above 60 years	19 (28.36%)	13 (39.39%)	= 0.2686
Systolic Blood Pressure (Mean ± SD) [mm Hg]	151.8±18.68	150.4±16.03	=0.7132
Normal (<120 mmHg), n (%)	06 (8.95%)	02 (6.06%)	= 0.6181
Pre HTN (120-139 mmHg), n (%)	15 (22.38%)	07 (21.21%)	= 0.8949
Stage 1 HTN (140-159 mmHg), n (%)	37 (55.22%)	20 (60.60%)	= 0.6112
Stage 2 HTN (≥160 mmHg), n (%)	09 (13.43%)	04 (12.12%)	= 0.8554
Diastolic Blood Pressure (Mean ± SD) [mm Hg]	96.55±10.78	94.90±11.28	= 0.4801
Normal (< 80 mmHg), n (%)	05 (7.46%)	03 (9.09%)	= 0.7786
Pre HTN (80-89 mmHg), n (%)	17 (25.37%)	05 (15.15%)	= 0.2484
Stage 1 HTN (90-99 mmHg), n (%)	37 (55.22%)	21 (63.63%)	= 0.4253
Stage 2 HTN (≥100 mmHg), n (%)	08 (11.94%)	04 (12.12%)	= 0.9793

Table-1: Baseline demographic and clinical characteristics of hypertensive patients (n=100).

Co-morbidities	Male [n=67]	Female [n=33]	Total [n=100]	Percentage (%)
Diabetes Mellitus	08 (11.94%)	04 (12.12%)	12	12
Other Cardiovascular diseases	06 (8.95%)	06 (18.18%)	12	12
Renal diseases	05 (7.46%)	02 (6.06%)	07	7
Liver Diseases	02 (2.98%)	01 (3.03%)	03	3
Hypothyroidism	03 (4.47%)	02 (6.06%)	05	5
Hyperthyroidism	02 (2.98%)	-	02	2
Lung disorders	05 (7.46%)	02 (6.06%)	07	7
Acid peptic disease	16 (23.88%)	09 (27.27%)	25	25
Obesity/overweight	08 (11.94%)	06 (18.18%)	14	14
Dyslipidemia	27 (40.29%)	14 (42.42%)	41	41
Other diseases	12 (17.91%)	05 (15.15%)	17	17

Table-2: Co-morbid conditions among hypertensive subjects

Table 3 shows the mono and combination therapies for the treatment of hypertension. As per present study, most

Treatment	No., Percentage [n=100]
Mono-therapy	29 (29%)
ACE Inhibitors (ACEIs)	5 (5%)
Angiotensin Receptor Blocker (ARBs)	6 (6%)
Diuretics	8 (8%)
Calcium Channel Blockers	4 (4%)
Beta Blockers	2 (2%)
Alpha Blockers	01 (1%)
Alpha 2 Agonists	01 (1%)
Potassium Channel Openers	-
Nitrates	02 (2%)
Two-drugs regimen	35 (35%)
Angiotensin receptor blockers + Diuretics	6 (6%)
Dihydropyridine Calcium channel blockers + β -blockers	2 (2%)
Diuretics + Calcium channel blockers	2 (2%)
ACE inhibitors + Diuretics	8 (8%)
ACE inhibitors + Dihydropyridine Calcium channel blockers	5 (5%)
Diuretics + β -blockers	2 (2%)
Diuretics + Diuretics [potassium sparing diuretics with thiazides]	2 (2%)
Calcium channel blockers + ARBs	4 (4%)
ACEIs/ARBs + β -blockers	2 (2%)
Calcium channel blockers + α -agonists	1 (1%)
Alpha Blockers + Diuretics	1 (1%)
ACEs + ARBs	0
β -blocker + central acting (clonidine)	0
β -blocker + nondihydropyridine CCB	0
Three Drugs Regimen	11 (11%)
CCBs + ACEIs/ARBs + Diuretics	5 (5%)
ARBs + Diuretic + Diuretic	2 (2%)
ACEIs/ARBs + BBs + CCBs	3 (3%)
ACEIs/ARBs + BBs + Diuretics	1 (1%)
Four Drugs Regimen	02 (2%)
Diuretics + Calcium channel blockers + β -blockers	1 (1%)
Angiotensin receptor blockers + diuretics + Calcium channel blockers	1 (1%)

Table-3: Antihypertensive medications used by hypertensive patients (males and females) in mono and combination therapies

of the physicians prescribed two-drug combination (35%) to control BP followed by monotherapy (29%), three-drug combination (11%) and four-drug combination (2%). Diuretics (8%) are most widely prescribed drugs followed by ARBs (6%), ACE Inhibitors (5%) and calcium channel blockers (4%) as monotherapy. In some cases beta blockers (2%) and alpha agonists (1%) also prescribed. Monotherapy of nitrates was also documented in 2% cases.

Two drugs regimen was prescribed in 35% of the hypertensive patients. ACE inhibitor (s) + diuretics combination (8%) was mostly used in two drug combination therapy followed by angiotensin receptor blockers + diuretics combination (6%) and ACE inhibitors + dihydropyridine calcium channel blockers (5%). There was different other combinations also prescribed in the hypertensive patients with or without co-morbidities like dihydropyridine calcium channel blockers + β -blockers (2%), calcium channel blockers + ARBs (4%), Diuretics + β -blockers (2%), ACEIs/ARBs + β -blockers (2%), diuretics + diuretics [potassium sparing diuretics with thiazides] (2%) and calcium channel blockers + alpha agonists (1%). None of the hypertensive patients was prescribed ACEs + ARBs, β -blocker + central acting (clonidine) and β -blocker + non-dihydropyridine CCB in combination [Table 3].

Three antihypertensive drugs regimen was prescribed in 11% of the hypertensive patients. Three drugs combination as an antihypertensive was mainly tried CCBs+ ACEIs/ARBs+ Diuretics (5%) followed by ACEIs/ARBs + BBs + CCBs (3%), and ARBs + Diuretic + Diuretic (2%). In few prescriptions (2%) it was also observed that four drugs regimen like ARBs+ Diuretics+ CCBs combinations (1%) also prescribed in uncontrolled hypertensive patients (Table 4). Majority of the patients were prescribed combination anti-HTN drugs with other drugs (78%) may be due to address associated co-morbidities.

Among the combination therapy olmesartan/amlodipine/HCTZ, valsartan/amlodipine/ (hydrochlorothiazide) HCTZ, candesartan/HCTZ, losartan/HCTZ, olmesartan/HCTZ, telmisartan/HCTZ, metoprolol tartrate/HCTZ, amlodipine + atenolol, amlodipine + losartan, amlodipine + enalapril, metoprolol tartrate/HCTZ, spironolactone/HCTZ, atenolol + chlorthalidone, nebivolol + HCTZ, enalapril + HCTZ, lisinopril + HCTZ, ramipril + HCTZ e, telmisartan + HCTZ

Recommendations	Non-adherence rate (%)	Adherence rate (%)	P-Value
Recommendation 1	22%	78%	< 0.0001
Recommendation 2	35%	65%	< 0.0001
Recommendation 3	25%	75%	< 0.0001
Recommendation 4	39%	61%	= 0.0019
Recommendation 5	27%	73%	< 0.0001
Recommendation 6	08%	92%	< 0.0001
Recommendation 7	-	-	-
Recommendation 8	12%	88%	< 0.0001
Recommendation 9	24%	76%	< 0.0001
Recommendation 10	38%	62%	= 0.0019
Average	25%	75%	< 0.0001

Table-4: Adherence to JNC-8 hypertension treatment recommendations

Rationality parameters	Non-adherence rate (%)	Adherence rate (%)	P-Value
Prescription rate stressing importance of lifestyle management	12%	88%	< 0.0001
Prescription rate with defined antihypertensive goals	22%	78%	< 0.0001
Dose strength mentioned rate	-	100%	-
Dose schedule mentioned rate	-	100%	-
Ban drug formulation prescription rate	-	0%	-
Debated rationality formulation prescription rate	85%	15%	< 0.0001
Generic versus brand name prescription rate	6%	94%	< 0.0001
Fixed dose combination versus combination prescription rate	83%	17%	< 0.0001

Table-5: Evaluation of rational drug therapy

and losartan + hydrochlorothiazide were found maximally prescribed in our study population. Amlodipine+ HCTZ + telmisartan, amlodipine + HCTZ + olmesartan and amlodipine + HCTZ + telmisartan + metoprolol were the frequently prescribed triple and four drug combinations, respectively. No combination of ACEIs + ARBs was prescribed in any prescription.

A comparison of residents' adherence by specialty to each JNC 8 guideline recommendation is presented in Table 4. Adherence of JNC 8 guidelines among all study hypertensive participants while prescribing medications varied between 62% to 92%, with an average of 75%. The least adherence (61%) was to recommendation 4 and 10 to initiate pharmacologic treatment in the population aged ≥ 18 years with chronic kidney disease to lower BP to goal of less than 140/90 followed by 62% adherence if goal BP cannot be reached with 2 drugs, add and titrate a third drug from the list provided. None of the patients was prescribed ACEI and an ARB together. However, 73% of the prescriptions were adherent to recommendation 5 to initiate pharmacologic treatment in the diabetes population.

The overall rate of adherence was 06/22 (27.27%) in pre-hypertension; 92% in stage 1 hypertension; and 78% in stage 2 hypertension patients. Almost 100% adherence rate among the patients of hypertensive emergency and urgency with the JNC 8 guidelines was noticed.

The rationality of prescription pattern of anti-hypertensive was also evaluated. The average number of drugs prescribed to each patient was 4-6 (64%). About 88% prescriptions had stressed importance of lifestyle management. About 225 of the prescription did not defined antihypertensive goals. None of the prescriptions mentioned ban drug formulation(s). Still 15% of the prescriptions had suggested combined drugs with debated rationality formulations. Only 6% of the prescription mentioned generic names of medicines. FDCs were prescribed more (83%) than 17% of combined prescribed drug(s) [Table 5].

DISCUSSION

Hypertension is a chronic disease requiring lifelong treatment. This observational study analysed the prescribing pattern in hypertensive patients and its adherence with JNC 8 guidelines for the management of hypertension, attending the outpatient department of General Medicine at Dr B C Roy Hospital, Haldia, West Bengal. Choice of an antihypertensive drug

should be driven by likely benefit in an individual patient, taking into account concomitant diseases such as diabetes mellitus, problematic adverse effects of specific drugs, and cost. The overall goal of treating hypertension is to reduce hypertension associated morbidity and mortality.¹³

Out of 100 hypertensive patients in present study 67 was males (67%) with a M:F ratio of 2.03:1. Mean age among male participants was less (55.29 \pm 16.48) in comparison to female hypertensive (59.30 \pm 11.55). The results of this study in line with study by Romday R et al (2016)¹³ which suggests that hypertension is more prevalent in males (59.8%), compared to females (40.2%). The above pattern is analogous to studies conducted by (Jhaj et al¹⁴; Malhotra et al¹⁵; Kothari et al¹⁶; Murti et al¹⁷) in India and Jeanette Sessoms et al (2015)¹⁸ in African Americans. However the above pattern is anomalous to other studies conducted by (Tiwarei et al¹⁹; Surapaneni et al²⁰) in India, Pittrow et al²¹ in Germany and Lee et al²² in China have reported higher prevalence of hypertension in females than in males. This study also reveals that hypertension is more prevalent in elderly patients belonging to age group 40-60 or more. Study conducted by Romday et al¹³ and Tiwarei et al¹⁹ found most common age group 50-59 years (33.3%) followed by 60-69 years and 40-49 years (26.7%).

Present study results showed diabetes mellitus (11.94%, males; 12.12%, females), other cardiovascular diseases (8.95%, males; 18.18%, females), acid peptic disease (23.88%, males; 27.27%, females), obesity (11.94%, males; 18.18%, females), and dyslipidemia (40.29%, males; 42.42%, females) are the most common co-morbidities in hypertension patients. Dyslipidemia was noted much more common associated disorders among newly diagnosed hypertensives of either sex. Present study results fall in line of the study by Romday R et al (2016).¹³ Study done by Amira et al²³ and Kothari et al¹⁶ found 36.6% and 47.72% patients respectively were suffering with comorbid conditions. Sakthi S et al²⁴ reported diabetes mellitus (35%) as the most frequent co-morbidity followed by asthma (5%) and ischemic heart disease (1.6%). Kothari N et al, reported majority of the patients were suffering from hypertension with diabetes mellitus (37.49%) followed by other associated conditions like ischemic heart diseases (7.12%), congestive heart failure (2%), and chronic kidney diseases (1.11%).¹⁶ Pai et al reported diabetes mellitus (47.5%), ischemic heart disease (16.5%), renal diseases (7.5%) and cardiovascular

accidents (16%) as concurrent diseases in his study.²³

As per present study, most of the physicians prescribed two-drug combination (35%) to control BP followed by monotherapy (29%), three-drug combination (11%) and four-drug combination (2%). Diuretics (8%) are most widely prescribed drugs followed by ARBs (6%), ACE Inhibitors (5%) and calcium channel blockers (4%) as monotherapy. In some cases beta blockers (2%) and alpha agonists (1%) also prescribed. Monotherapy of nitrates was also documented in 2% cases.

Two drugs regimen was prescribed in 35% of the hypertensive patients. ACE inhibitor (s) + diuretics combination (8%) was mostly used in two drug combination therapy followed by angiotensin receptor blockers + diuretics combination (6%) and ACE inhibitors + diltiazem/calcium channel blockers (5%). It also shows that most frequently prescribed classes of drugs are thiazides alone or in combination. Since the eighth report of Joint National Committee (JNC 8) on detection, evaluation prevention and treatment recommends the use of ACEIs, ARBs, thiazide diuretic, and CCBs alone or in combination for the management of early stage hypertension, thus suggesting that the above trend is in conformity to the recommendations of JNC 8 guidelines.²⁴ Hence this drug utilization data corroborates adherence to JNC 8 guidelines. However, the results of current study were not fully in accordance to the study of Tiwari et al as far as drug prescription rate of BBs is concerned.¹⁹ ACE inhibitors and ARBs prescription rates in their study were almost in comparison to present study. This might be because of recently gained popularity of ARBs and ACEIs. In combination therapy, a two drug combination consisting of BBs and CCBs was given to the majority of the patients like our study. The study of Dhanraj et al recorded highest prescription rates of ACE inhibitors (59%) followed by ARBs (52%), CCBs (29%), diuretics (27%), and BBs (14%).²⁷ Thiazides were the most preferred agents used, either as monotherapy or combination therapy in hypertensive patients with or without comorbidities in accordance to our study.

Adherence of JNC 8 guidelines among all study hypertensive participants while prescribing medications varied between 62% to 92%, with an average of 75%. The least adherence (61%) was to recommendation 4 and 10 to initiate pharmacologic treatment in the population aged ≥ 18 years with chronic kidney disease to lower BP to goal of less than 140/90 followed by 62% adherence if goal BP cannot be reached with 2 drugs, add and titrate a third drug from the list provided. None of the patients was prescribed ACEI and an ARB together. However, 73% of the prescriptions were adherent to recommendation 5 to initiate pharmacologic treatment in the diabetes population.

The overall rate of adherence was 06/22 (27.27%) in pre-hypertension; 92% in stage 1 hypertension; and 78% in stage 2 hypertension patients. Almost 100% adherence rate among the patients of hypertensive emergency and urgency with the JNC 8 guidelines was noticed.

Drugs are often used in combination to achieve a preferred therapeutic goal or to treat coexisting diseases. Because of

the risk related to concomitant use of drugs, co-medication has become a general concern and an important concept in term of prescribing appropriateness. Some combinations may result in undesired pharmacodynamic or pharmacokinetic interactions, resulting in under-treatment or harmful effects. The consequences of drug-drug interactions (DDIs) can range from no untoward effects at all, to drug-related mortality.^{28,29}

Strengths and Limitations of the Study

Our study supports the usefulness of the awareness to an adherence model and affords valuable information on the implementation of an important guideline in India. This study had some limitations also. Data were collected from only one institution, therefore population is relatively homogenous. Due to small sample size, variability and vagueness should be noted as limitations. A larger sample size would produce more detailed, robust, and explanatory assessments. Large studies involving heterogeneous population are required. Secondly, the study was conducted during only the summer months and over a short duration. Extending the study period and expanding the study to include fall or winter months may provide input for comparison to determine if seasons impact BP control.

Despite these limitations, the strength of the data collected is such that it revealed several important aspects of the antihypertensive drug utilization pattern and adherence of these drugs to JNC-VIII guidelines in different co-morbid conditions.

CONCLUSION

Present results reveals that antihypertensive medication adherence to JNC-8 recommendations is suboptimal. Therefore, physicians should follow JNC-8 guidelines to improve the patients care because suboptimal adherence leads to adverse clinical outcomes. In conclusion, present study demonstrated that physicians are not completely adhering to standard guidelines while treating hypertension with co-morbid conditions.

Despite evidence-based recommendations by JNC 8, provider adherence in AAs has room for improvement. Provider pharmacologic choices and lifestyle modification recommendations are major components to blood pressure control in this population. Thiazide diuretics are recommended as initial monotherapy and in combination therapy for Indian hypertensive patients. ACEIs, ARBs and CCBs are recommended as an acceptable alternative to thiazide diuretics. Prescribers have demonstrated a preference in prescribing ACEIs and ARBs in monotherapy. Adherence rates to JNC 8 were adequate in Stage 1, hypertensive emergency and urgency and inadequate in case of pre-HT and Stage 2 HT. BBs were under prescribed as this is not in the first line drug for initial management of hypertension. Polypharmacy, FDCs, debated rationality anti-HT combinations prescribing, were some of the common pharmacologically considered irrationality noticed in present study.

ACKNOWLEDGEMENT

ICMR STS-2018, Ref. ID: 2018-02040

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 02-09-2019; **Accepted:** 30-09-2019; **Published:** 28-10-2019

**GAMBARAN POLA PENGGUNAAN OBAT ANTIHIPERTENSI PADA
PASIEH HIPERTENSI DI INSTALASI RAWAT INAP RSUP SANGLAH
DENPASAR TAHUN 2016****Luh Sonya Astana Putri¹, Bagus Komang Satriyasa², I Made Jawi²**¹Program Studi Pendidikan Dokter Fakultas Kedokteran Universitas Udayana²Bagian Farmakologi Fakultas Kedokteran Universitas Udayana**ABSTRAK**

Tingginya angka kejadian hipertensi berdampak terhadap meningkatnya morbiditas dan mortalitas masyarakat. Diperlukan manajemen yang tepat untuk mengontrol hipertensi, salah satunya dengan pemberian terapi farmakologis antihipertensi. Penelitian ini bertujuan untuk mengetahui gambaran pola penggunaan obat antihipertensi di Instalasi Rawat Inap RSUP Sanglah Denpasar tahun 2016. Penelitian ini dirancang dengan metode deskriptif *cross-sectional*. Subjek penelitian dipilih menggunakan teknik *consecutive sampling* dari populasi terjangkau yang memenuhi kriteria inklusi periode April-Desember 2016. Data bersumber dari rekam medis pasien dan dianalisis secara statistik deskriptif. Hasil penelitian menunjukkan bahwa dari 56 subjek penelitian sebanyak 60,7% mendapat politerapi dan 39,3% mendapat monoterapi. Golongan obat yang paling banyak digunakan untuk monoterapi adalah ACE-I dan untuk politerapi yaitu golongan ACE-I dan CCB. Berdasarkan derajat hipertensi, sebagian besar monoterapi diberikan pada pasien dengan hipertensi stadium 1 dan politerapi pada pasien dengan hipertensi stadium 2. Pada penelitian ini disimpulkan bahwa penatalaksanaan farmakologis antihipertensi sebagian besar dalam bentuk politerapi. Penelitian ini diharapkan dapat menjadi acuan dalam pemberian terapi farmakologis antihipertensi pada pasien hipertensi.

Kata Kunci : *Hipertensi, pola penggunaan, obat antihipertensi, rawat inap.***ABSTRACT**

The high number of hypertension affects to the morbidity and mortality increase in society. It needs correct management to control hypertension; one of them is by giving anti-hypertension pharmacologists therapy. This study purpose is to understand the illustration of anti-hypertension medicine pattern in Inpatient Care Facility at Sanglah General Hospital Denpasar 2016. This study uses cross-sectional descriptive method. The subject of this study is chosen by consecutive sampling technique from accessible populations which have fulfilled inclusion criteria during April-December 2016. The data source is from patients medical records and analyzed descriptive statistically. The result of this study shows from 56 research subjects, 60.7% has got polytherapy and 39.3% has got monotherapy. The most used drugs category for monotherapy is ACE-I and polytherapy are ACE-I and CCB. Based on hypertension severity, most of monotherapy are given to hypertension stage 1 and polytherapy to hypertension stage 2. It can be concluded that the management of anti-hypertension pharmacologists are mostly in polytherapy. The research is expected to be a reference in giving anti-hypertension pharmacologists therapy to hypertension patients.

Keywords: *Hypertension, usage pattern, anti-hypertension medicine, inpatient.*

PENDAHULUAN

Hipertensi perlu mendapat perhatian khusus dari masyarakat mengingat dampak yang ditimbulkan baik dalam jangka pendek maupun jangka panjang, salah satunya adalah upaya penanganan antihipertensi dengan terapi pemberian farmakologis antihipertensi secara tepat sebagai suatu langkah yang strategis.¹

Berdasarkan penelitian mengenai penggunaan obat antihipertensi sebelumnya menyebutkan bahwa evaluasi ketepatan obat pada penggunaan obat antihipertensi di RSUP Dr. Kariadi Semarang menunjukkan 2% tidak tepat indikasi, 19% tidak tepat obat, dan 38% tidak tepat pasien.² Penelitian yang dilakukan di bangsal saraf RSUP Dr. M. Djamil Padang pada 24,24% pasien hipertensi dengan stroke hemoragik mendapatkan ketidaktepatan pemilihan obat terutama kombinasi antihipertensi dari golongan yang sama.³ Hal yang sama juga terjadi pada penelitian yang dilakukan oleh Wulandari dkk.⁴ pada beberapa kasus obat antihipertensi yang diberikan tidak sesuai dengan karakteristik penyakit pasien hipertensi.

Penggunaan obat antihipertensi yang tidak tepat dapat menyebabkan spektrum toksisitas, kegagalan terapi pengobatan, biaya pengobatan yang tinggi, komplikasi hingga kematian pasien, serta menghambat mutu pelayanan kesehatan itu sendiri. Sehingga dalam strategi pemilihan obat antihipertensi senantiasa dilakukan sesuai standar, hal ini harus diterapkan di seluruh pelayanan kesehatan yang terdapat di Indonesia termasuk di Provinsi Bali.⁵

Uraian latar belakang di atas menunjukkan bahwa penting untuk mengkaji gambaran pola penggunaan antihipertensi pada pasien hipertensi dalam sebuah penelitian yang dilakukan di Instalasi Rawat Inap RSUP Sanglah Denpasar tahun 2016 sebagai rumah sakit rujukan utama di Provinsi Bali.

BAHAN DAN METODE

Penelitian ini menggunakan metode penelitian deskriptif dengan rancangan *cross-sectional* untuk mengetahui karakteristik pasien, jenis terapi berupa monoterapi dan politerapi serta golongan obat antihipertensi yang digunakan.

Data penelitian berupa rekam medis pasien hipertensi yang dipilih dengan menggunakan teknik *consecutive sampling* dari populasi terjangkau yang memenuhi kriteria inklusi dan kriteria eksklusi dengan besar sampel ditentukan menggunakan rumus statistik. Kriteria inklusi yaitu subyek berusia ≥ 18 tahun yang menjalani rawat inap pertama kali di RSUP Sanglah tahun 2016 dengan hipertensi tanpa atau disertai penyakit penyerta dan mendapat terapi farmakologis antihipertensi.

Data yang terkumpul akan menjalani proses pengolahan dan analisis data kemudian disajikan dalam bentuk tabel distribusi frekuensi

HASIL

Distribusi Karakteristik Subyek Penelitian

Penelitian ini dilakukan di Instalasi Rekam Medis RSUP Sanglah dengan subyek penelitian yang terkumpul sebanyak 56 pasien.

Tabel 1 menunjukkan distribusi karakteristik subyek penelitian didapatkan lebih banyak subyek penelitian berjenis kelamin laki-laki dibanding perempuan. Kategori usia subyek penelitian paling tinggi di rentang usia 46 sampai dengan 65 sebesar 48,2%. Berdasarkan derajat hipertensi sebagian besar berada pada kategori derajat hipertensi stadium 2 yaitu sebesar 66,1%. Distribusi penyakit penyerta pada subyek penelitian, sebanyak 39,3% menderita hipertensi dengan penyakit penyerta seperti stroke, diabetes melitus tipe 2, gagal ginjal kronik dan penyakit jantung koroner.

Tabel 1. Karakteristik Subyek Penelitian.

No	Variabel	Jumlah (%) Total (N=56)
1.	Jenis Kelamin	
	Laki-laki	30 (53,6)
	Perempuan	26 (46,4)
2.	Usia	
	18-40 tahun	10 (17,9)
	41-59 tahun	25 (44,6)
	≥60 tahun	21 (37,5)
3.	Derajat Hipertensi	
	Hipertensi Stadium 1	19 (33,9)
	Hipertensi Stadium 2	37 (66,1)
4.	Adanya Penyakit Penyerta	
	Hipertensi dengan penyakit penyerta	22 (39,3)
	Hipertensi tanpa penyakit penyerta	34 (60,7)

Distribusi Pola Penggunaan Obat Antihipertensi

Tabel 2 menunjukkan 22 (39,3%) dari 56 subyek penelitian mendapat monoterapi dan 34 orang (60,7%) lainnya

mendapat politerapi, dimana berdasarkan derajat hipertensi subyek penelitian dengan hipertensi stadium 1 lebih banyak mendapatkan monoterapi yaitu sebanyak sepuluh orang (17,9%), sedangkan pada subyek penelitian dengan hipertensi stadium 2, sebagian besar mendapat politerapi yaitu sebanyak 25 orang (44,6%).

Golongan ACE-I paling banyak diberikan pada monoterapi yaitu 12 orang (21,4%), diikuti oleh golongan CCB, β -bloker, ARB, dan sisanya satu orang diberikan diuretik. Sedangkan untuk politerapi, sebagian besar diberikan terapi kombinasi golongan 2 obat yaitu CCB dan ACE-I pada 22 (39,3%) subyek penelitian.

Terapi kombinasi lain meliputi kombinasi CCB dan ARB diberikan pada empat orang (7,1%), kombinasi β -bloker dan ACE-I pada dua orang (3,6%) pasien. Satu orang pasien (1,8%) masing-masing diberikan pada terapi kombinasi dua obat dan tiga obat antihipertensi.

Tabel 2. Distribusi Pola Penggunaan Obat Antihipertensi

Jumlah Obat	Golongan Obat Antihipertensi	Derajat Hipertensi Jumlah (%)		Jumlah (%) Total (n=56)
		Stadium 1	Stadium 2	
Monoterapi	Diuretik	0 (0)	1 (1,8)	1 (1,8)
	β -bloker	1 (1,8)	1 (1,8)	2 (3,6)
	ACE-I	4 (7,1)	8 (14,3)	12 (21,4)
	ARB	2 (3,6)	0 (0)	2 (3,6)
	CCB	3 (5,4)	2 (3,6)	5 (8,9)
Politerapi 2 Obat	Diuretik, CCB	0 (0)	1 (1,8)	1 (1,8)
	Diuretik, ARB	0 (0)	1 (1,8)	1 (1,8)
	β -bloker, ACE-I	0 (0)	2 (3,6)	2 (3,6)
	β -bloker, ARB	1 (1,8)	0 (0)	1 (1,8)
	CCB, ACE-I	4 (7,1)	18 (32,1)	22 (39,3)
	CCB, ARB	3 (5,4)	1 (1,8)	4 (7,1)
3 Obat	Diuretik, CCB, ACE-I	0 (0)	1 (1,8)	1 (1,8)
	β -bloker, ACE-I, CCB	0 (0)	1 (1,8)	1 (1,8)
	β -bloker, ARB, CCB	1 (1,8)	0 (0)	1 (1,8)

PEMBAHASAN

Hasil penelitian ini sesuai dengan penelitian Primasari dan Artini, yang menunjukkan bahwa subyek penelitian lebih banyak mendapatkan politerapi dibanding monoterapi.⁴

Terapi farmakologis hipertensi diawali dengan pemakaian obat tunggal karena monoterapi mampu menurunkan TD sistolik sekitar 7-13 mmHg dan diastolik sekitar 4-8 mmHg.⁶

Jika target TD tidak tercapai dalam waktu satu bulan pengobatan, maka dapat dilakukan peningkatan dosis obat awal atau penambahan golongan obat lain yang berasal dari terapi lini pertama dan kedua dengan meminimalkan efek samping interaksi obat.⁷

JNC 8 juga menekankan bahwa kombinasi dua obat dosis rendah direkomendasikan untuk kondisi TD >20/10 mmHg di atas target. Sehingga jika dikaitkan pada penelitian ini sebagian besar subyek penelitian yang menderita hipertensi stadium 2 atau TD >20/10 mmHg diatas normal, sehingga rasional atau tepat indikasi untuk mendapat politerapi.⁸

Golongan obat antihipertensi yang paling banyak digunakan adalah golongan ACE-I, diikuti oleh golongan CCB dan ARB. Hasil penelitian ini sesuai dengan penelitian yang dilakukan oleh Ramadhan dkk.⁹ Berdasarkan JNC 8 yang diperbarui terdapat empat golongan obat yang direkomendasikan pada terapi lini pertama yaitu diuretik thiazide, β -blockers, CCB, ACE-I, dan ARB.⁷

ACE-I bekerja menghambat enzim yang menghidrolisis angiotensin I menjadi angiotensin II dan menurunkan TD melalui penurunan resistensi vaskular perifer.⁵

ACE-I lebih banyak dipilih karena dari segi keamanan ACE-I tidak menimbulkan efek samping metabolik pada penggunaan jangka panjang, kelompok ACE-I menyebabkan vasodilatasi pada arteriola efferent ginjal dan mengurangi proteinuria sehingga memiliki efek perlindungan ginjal.¹⁰ Selain

itu ACE-I juga berperan dalam mencegah mortalitas pasien resiko tinggi komplikasi jantung. Efek samping dari golongan ACE-I paling khas berupa batuk kering dan angiodema.⁷

Golongan ARB menghambat secara langsung reseptor angiotensin yang lebih selektif yaitu AT1. Pada pasien yang mengalami efek samping dari ACE-I maka terapi yang disarankan adalah ARB.⁵ Namun dari segi biaya ARB sekitar 45 kali lebih mahal dari golongan ACE-I sehingga kurang rasional untuk diberikan pada pasien.¹¹

CCB biasanya digunakan untuk terapi hipertensi dengan jantung koroner dan diabetes melitus.⁷ Mekanisme kerja dari golongan ini dengan cara menghambat influks kalsium di otot polos arteri sehingga terjadi vasodilatasi dan menurunkan resistensi perifer.⁵

Hasil penelitian ini hanya satu orang subyek yang mendapat monoterapi diuretik thiazide. Hal ini berbeda dengan penelitian yang dilakukan oleh Fitrianto dkk.¹² menyatakan bahwa golongan obat antihipertensi yang paling sering digunakan adalah golongan diuretik thiazide. Diuretik jenis thiazide efektif dalam menurunkan TD sebesar 10-15 mmHg dengan menguras simpanan natrium tubuh. Adapun efek samping dari penggunaan diuretik thiazide adalah gangguan metabolik.⁵

Golongan β -bloker berdasarkan JNC 8 tidak digunakan sebagai terapi lini pertama kecuali ada indikasi tertentu sesuai mekanisme kerjanya. Hasil penelitian menunjukkan dua subyek penelitian mendapatkan monoterapi dengan β -bloker dengan rincian satu orang dengan komplikasi stroke dan sisanya mempunyai penyakit gagal ginjal kronik. Menurut JNC 8, golongan ini bisa digunakan sebagai terapi primer pada pasien yang baru mengalami serangan stroke, pasien riwayat gagal jantung, angina pectoris dan infark miokard.⁷

Penelitian lain menyatakan pengobatan dengan β -bloker dapat

menurunkan angka kematian pada pasien gagal ginjal kronik dengan gagal jantung sistolik kronis, tetapi kelemahan dalam penelitian ini yaitu tidak mendeskripsikan penyakit gagal jantung sehingga indikasi pemberian β -bloker pada monoterapi tidak diketahui.¹³

Pemberian politerapi kepada subyek penelitian melibatkan kombinasi dua dan tiga golongan obat dengan sebagian besar subyek penelitian mendapatkan kombinasi CCB dan ACE-I atau kombinasi CCB dan ARB. Hal ini sejalan dengan penelitian Setriana dkk.³ Semua kombinasi obat tersebut sudah sesuai dengan *guideline* JNC 8 karena berasal dari golongan obat yang berbeda.

Menurut Kandarini, golongan CCB dihidropiridin dapat menyebabkan diuresis dan natriuresis akut, hal ini akan mengaktifkan respon RAAS yang akan dihambat oleh ACE-I dan ARB, sehingga menurunnya angiotensin II menyebabkan efek CCB semakin poten.¹⁴

Kombinasi ACE-I atau ARB dengan CCB lebih banyak diberikan pada pasien hipertensi karena bisa ditoleransi dengan baik pada awal pengobatan dan lebih unggul dari kombinasi dengan diuretik dalam menghambat stimulasi RAAS, serta mengurangi stres oksidatif, rigiditas arteri, menurunkan risiko progresifitas stroke dan penebaran vaskular.¹⁵

Sebuah penelitian mengenai selisih penurunan TD sistolik dan diastolik sebelum dan setelah menggunakan obat selama tiga bulan pada pasien hipertensi derajat 1 dan 2 menyatakan kombinasi dua obat ACE-I dengan CCB lebih baik dibandingkan CCB dengan diuretik thiazide, dan kombinasi ARB dengan diuretik lebih baik daripada kombinasi CCB dengan diuretik.¹⁶

Kombinasi CCB dengan diuretik diberikan pada satu subyek penelitian. Pada kombinasi ini terjadi efek aditif sebagian karena sifat antara farmakologi kedua obat tumpang tindih dimana CCB juga bersifat walaupun tidak sebesar efek natriuretik golongan diuretik.⁴ Kombinasi

ini umumnya dapat ditoleransi dengan baik, karena dapat mengurangi timbulnya edema akibat CCB, mengurangi morbiditas dan mortalitas kardiovaskular serta stroke pada lansia. Efek samping yang sering dilaporkan adalah hypokalemia.¹⁶

Kombinasi diuretik dan ARB diberikan pada satu orang pasien, dimana terjadi ekskresi air dan sodium oleh diuretik thiazide yang akan dikompensasi oleh RAAS sehingga membatasi efektivitas thiazide, dengan adanya agen penghambat RAAS maka kerja diuretik akan optimal.¹⁴

Hasil penelitian ini juga menunjukkan tiga orang subyek diberikan kombinasi ACE-I atau ARB dengan β -bloker, beberapa penelitian membuktikan bahwa dengan menambahkan β -bloker ke terapi ACE-I sebelumnya hanya memberikan sedikit efek antihipertensi dibanding terapi tunggal dengan ACE-I dalam menurunkan TD karena mekanisme kerja ACE-I pada renin bertentangan dengan penghambatan renin yang diinduksi oleh β -bloker.¹⁰

JNC 8 menyatakan jika target TD tidak bisa dicapai menggunakan kombinasi dua golongan antihipertensi maka dibutuhkan lebih dari tiga obat untuk mencapai target TD. Mazza dkk.¹⁷ didukung oleh persetujuan FDA menyatakan bahwa *Fix Dose Triplet Combination* perindopril, indapamide dan amlodipine efektif dan aman untuk menurunkan TD pada pasien yang belum terkontrol dengan dua kombinasi obat antihipertensi. Hal ini dijadikan acuan dalam memilih kombinasi tiga obat rasional dari golongan penghambat RAAS, diuretik, dan CCB yang terdapat pada penelitian yang dilakukan oleh Primasari dan Artini dan penelitian ini.⁴

Subyek penelitian sebanyak dua orang menerima kombinasi CCB, β -bloker dan penghambat RAAS, hal ini dikatakan rasional atau tepat pemilihan obat karena berdasarkan *Guideline* JNC 8, β -bloker merupakan lini kedua pengobatan

hipertensi dimana golongan ini akan ditambahkan dalam terapi pasien ketika terapi lini pertama sudah ditambahkan dari golongan berbeda atau sebagai pilihan terakhir dalam pengobatan hipertensi ketika TD tidak mencapai target dengan terapi lini pertama.⁸

Pola penggunaan obat antihipertensi monoterapi pada derajat hipertensi stadium 1 sudah tepat, karena terapi farmakologi antihipertensi dapat dimulai dari monoterapi pada pasien hipertensi stadium 1. Beberapa kasus pemberian monoterapi tidak bisa mengontrol tekanan darah pasien atau kondisi pasien yang mengindikasikan pemberian politerapi pada beberapa subyek penelitian dengan tujuan memperbaiki kontrol tekanan darah.

Subyek penelitian dengan hipertensi stadium 2 sebagian besar subyek penelitian mendapatkan politerapi. Sisanya 12 subyek penelitian mendapatkan monoterapi, hal ini tidak sesuai dengan JNC 8 yang merekomendasikan politerapi pada pasien dengan hipertensi stadium 2 atau TD > 20/10 mmHg di atas target. Jadi pada pasien dengan derajat hipertensi stadium 2, pemberian politerapi sudah tepat indikasi sedangkan pemberian monoterapi tidak sesuai dengan keadaan medis pasien, namun karena sumber penelitian yaitu rekam medis terbatas dan penelitian ini merupakan penelitian retrospektif dimana tidak dapat diwawancarai secara langsung paramedis yang berwenang mengenai indikasi medis lain yang mempengaruhi manajemen farmakologis antihipertensi dari subyek penelitian.⁹

Penelitian oleh Wana menyatakan bahwa antar kelas obat antihipertensi tunggal atau kombinasi relatif sama dalam menurunkan TD sistolik dan diastolik hipertensi stadium 1 dan 2. Kombinasi ARB dan diuretik, ACEI dan CCB, ACE-I dan diuretik thiazide lebih baik dibandingkan dengan kombinasi CCB dan diuretik thiazide pada hipertensi stadium 2 yang ditemukan pada salah satu subyek penelitian.¹⁰

Penjabaran diatas dapat dijadikan referensi terutama bagi klinisi dalam memilih jenis terapi serta golongan obat antihipertensi secara rasional sesuai dengan prinsip terapi farmakologis, indikasi pasien dan efektivitas antihipertensi masing-masing golongan obat antihipertensi.

Distribusi pola penggunaan obat antihipertensi pada subyek hipertensi dengan penyakit penyerta pada penelitian ini sudah sesuai dengan *Guideline JNC 8*. Pada subyek penelitian dengan stroke lebih banyak mendapatkan monoterapi dengan persentase golongan obat yang digunakan paling banyak yaitu ACE-I, hal ini sesuai dengan *guideline JNC 8* yang merekomendasikan golongan ACE-I dan diuretik untuk mencegah serangan stroke kembali.

Subyek penelitian dengan diabetes melitus lebih banyak mendapatkan politerapi meliputi kombinasi CCB dan ARB, CCB dan ACE-I, serta kombinasi β -bloker, ACE-I, CCB. Berdasarkan JNC 8, empat golongan obat antihipertensi yaitu ACE-I, ARB, CCB dan diuretik dapat dijadikan pilihan terapi untuk pasien hipertensi dengan DM tipe 2. ACE-I atau ARB lebih direkomendasikan dibanding golongan lain dan kombinasi diuretik dan β -bloker dihindari karena mempengaruhi metabolisme insulin.¹¹

Subyek penelitian dengan gagal ginjal kronik lebih banyak mendapatkan politerapi CCB dan ACE-I sisanya CCB dan ARB sedangkan pada monoterapi golongan CCB yang paling banyak digunakan. Dalam *guideline JNC 8* terapi awal dengan ACE-I atau ARB dengan atau tanpa kombinasi dengan CCB lebih baik dari golongan antihipertensi lain karena bersifat nefroprotektor.¹² Selain itu, subyek penelitian dengan penyakit jantung koroner mendapat monoterapi masing-masing dari golongan ACE-I dan CCB, sisanya yaitu satu orang subyek penelitian mendapatkan terapi kombinasi β -bloker dan ARB. Berdasarkan JNC 8, pada pengobatan hipertensi pada pasien dengan

penyakit arteri koroner direkomendasikan ACE-I, diuretik, β -blocker dan CCB sebagai terapi awal. Jika pasien sudah mengalami infark miokard untuk terapi awal dipilih β -blocker dan ACE-I atau ARB.⁷

SIMPULAN

Karakteristik pasien hipertensi di Instalasi Rawat Inap RSUP Sanglah Denpasar tahun 2016 lebih banyak laki-laki, kelompok usia 41-59 tahun, dengan hipertensi stadium 2 dan hipertensi tanpa penyakit penyerta.

Penatalaksanaan farmakologis antihipertensi sebagian besar dalam bentuk politerapi. Sedangkan golongan obat yang paling banyak digunakan adalah ACE-I. Berdasarkan derajat hipertensi, sebagian besar monoterapi diberikan pada pasien dengan hipertensi stadium 1 dan politerapi pada pasien dengan hipertensi stadium 2.

Hasil penelitian ini diharapkan dapat menjadi salah satu acuan dalam pemberian terapi farmakologis antihipertensi pada pasien hipertensi.

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